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Oxidative strategies in lignin chemistry: A new environmental friendly approach for the functionalisation of lignin and lignocellulosic fibers

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ABSTRACT

Novel processing methods and product concepts are required to extend the role of lignin for future biomass and biofuel applications in emerging platforms such as the biorefinery. The possible strategies of lignin valorisation are focused into two main directions, namely the selective functionalisation of the lignin polymer or in its oxidative depolymerization to get polyfunctional monomeric compounds. Here we report a panel of biocatalysis, organometallic catalysis, biomimetic catalysis and plasma oxidation processes developed by our research group for the activation of the environmental friendly oxidants oxygen and hydrogen peroxide in the oxidative functionalisation of lignin and lignin model compounds.

1. Introduction

Agricultural and forestry residues constitute a renewable source of lignocellulosic materials. Implementing concepts such as that of the biorefinery will allow the creation of high-value products that can improve profitability and can increase efficiency with respect to conventional mineral oil refinery. Despite the fact that the industrial use of biopolymers such as cellulose is considerable, lignin, the second most abundant biopolymer which accounts for 15–30% of biomass, is a under-utilized source of chemical energy. The use of lignin is nowadays still limited to thermovalorisation processes as filler in composites, component in binders and coatings, or, at a lower extent, surfactant/dispersant additives, whereas its potential as a source of valuable phenols in the production of high value-added biopolymers in alternative to petrol chemistry is largely unexploited. Thus, novel processing methods and product concepts are required to extend the role of lignin for future biomass and biofuel applications in emerging platforms such as the biorefinery. The chemical heterogeneity of lignin is one of the main reasons for the lack of valorisation of lignin residues that emerge from pulp and paper, and modern saccharification processes. Lignins are polyphenols characterized by a complex network of three main monomeric phenyl propanonic units bonded trough an array of different interunit bondings. The lack of a repetitive sequence, specific interunit bondings and specific subunits makes the structural characterization and upgrade of lignin a challenging task for the chemists (Scheme 1).

The most abundant bonding patterns in native lignins are the β-O-4′ aryl glycerol ether bond (45–48% in softwood) (Scheme 2a), the β-5 phenyl coumaran bond (9–12%) (Scheme 2b), the β–β′ pinoresinol (3%) (Scheme 2c), dibenzodioxocine 5-5′-α, β-O-4′ (5%) (Scheme 2d), the diphenyl ether 4-O-5′ (3, 5–8%) (Scheme 2e) and β-1′diphenyl ethane (7–10%) (Scheme 2f) [1]. Besides these substructures, lignan subunits such as furan and tetrahydro furofuran lignans, characterized by a β–β′ linkage between the two phenylpropanoid units, are also present in low amount. Moreover, lignins emerging from pulping processes contain appreciable amounts of structures such as 5-5′ and diphenylmethane that are recalcitrant to conventional oxidation treatments (Scheme 2g,h).

The possible strategies of lignin valorisation are focused into two main directions, namely the selective functionalisation of the lignin polymer in order to improve its compatibility and performance in composite and copolymer materials, or in alternative, in its oxidative polymerization to get polyfunctional monomeric compounds to be used as feed-stocks for polymer industry as an alternative to fossil fuels derived building blocks.

In this context special emphasis was devoted in the last years to the study of lignin oxidative functionalisation processes, mainly due to the presence of high amounts of side-chain aliphatic OH, terminal phenolic OH groups (Scheme 1) and reactive benzylic positions, that can be selectively modified.

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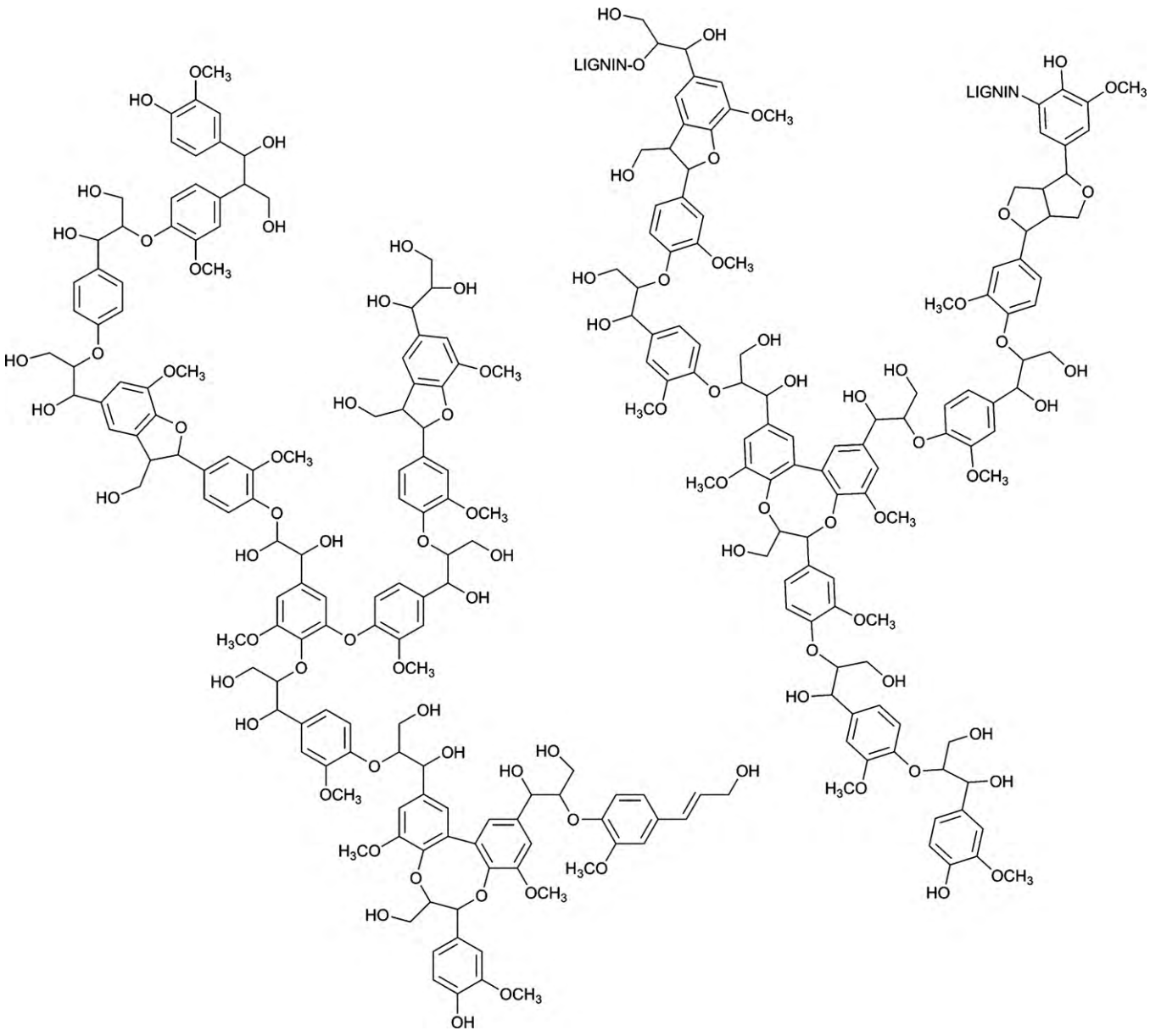


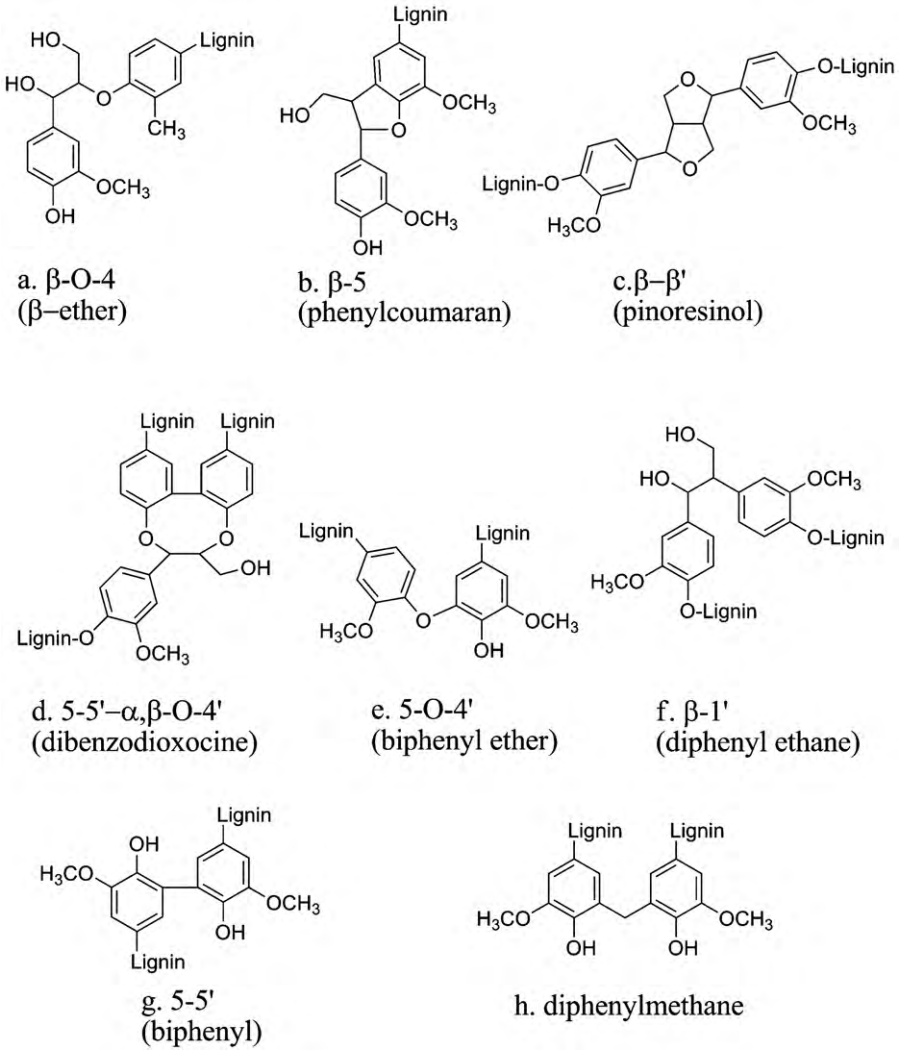
Scheme 1. Lignin structure.

Here we report a panel of oxidative processes by means of biocatalysis, organometallic catalysis, biomimetic catalysis and plasma processes developed by our research group for the activation of the environmental friendly oxidants oxygen (O_2) and hydrogen peroxide (H_2O_2) in the oxidative functionalisation of lignin and lignin model compounds.

2. Oxidation of lignin by biocatalysis processes

2.1. Laccase

Laccase, benzenediol:oxygen oxidoreductase 1.10:3.2, is a multicopper oxidase that performs the reduction of oxygen to water. The enzyme contains four copper centres, one type 1 Cu (T1), one type 2 Cu (T2) and a coupled binuclear type 3 (T3) Cu centre [2,3]. The T2 and T3 sites form a trinuclear Cu cluster onto which O_2 is reduced [4]. The T1 Cu atom oxidizes the reducing substrate and transfers electron to the T2 and T3 Cu atoms. Laccase is able to oxidize phenolic systems by an outer-sphere electron transfer process that generates a radical cation, which by fast deprotonation generates a reactive phenoxy radical [5]. The phenoxy radical intermediates formed during this process can further disproportionate or couple and consequently initiate lignin degradation [6]. Laccase shows a high thermal resistance (stable at 60 °C) [7], low substrate specificity and high oxidation rates that make this enzyme an ideal candidate for the development of efficient processes for lignin modification [7–9]. The redox potential of laccases depends on the fungal species that have been used for their production. The redox potential [versus NHE (normal hydrogen electrode)] varies from 430 mV for tree laccase from *Rhus vernicifera* to 780 mV for fungal laccase from *Polyporus versicolor* [10]. In any case the oxidation of substrates with blocked phenolic O–H, for example, methoxybenzene derivatives, is prevented by their high redox potential, and requires the presence of radical mediators such as 1-hydroxybenzotriazole (HBT) and 2,2-azinobis-3-ethyl-benzthiazoline-6-sulfonate (ABTS) [11–13]. In Scheme 3 the accepted mechanism for laccase oxidation of phenolic compounds is reported. Pathways B, C and D are not likely to occur due



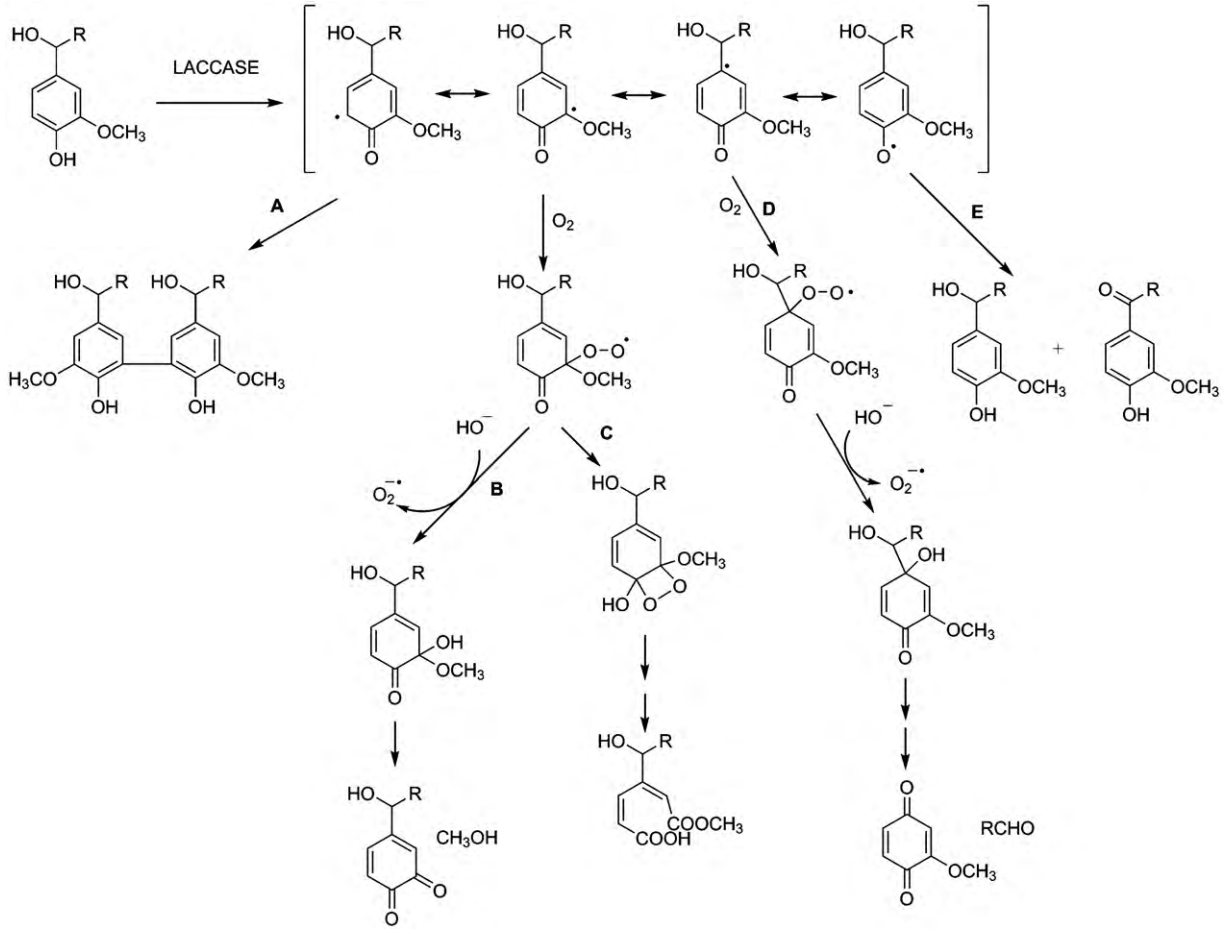
Scheme 2. Lignin interunit bondings.

to the slow kinetics of oxygen addition to phenoxy radical species [14]. The radical mediator, such as HBT, acts as a diffusible lignin oxidizing agents since it can access inner lignin structures in the cell wall as opposed to the relatively large enzyme [15].

In order to elucidate the delignification mechanism catalyzed by laccase, several studies have been carried out on both phenolic and non-phenolic monomeric, arylglycerol β-O-4 and β-1 ether lignin model compounds (see for example: [16] and [17]). The oxidation of condensed phenolic structures, such as 5-5′, α-5, diphenylmethane and stilbene units, is also an important tool to be achieved mainly because they are among the main units of high stable (and recalcitrant to oxidation) kraft lignin [18]. In order to elucidate the reactivity pattern of laccase mediator system toward kraft lignins, efforts have been devoted to study the oxidation of different condensed phenolic models with laccase and HBT [19]. For example, the oxidation of the 5-5′ condensed model dehydrocreosol **1** with laccase from *Trametes versicolor* both in the presence and in the absence of the radical mediators ABTS and HBT afforded products of alkyl side-chain oxidation (benzyl alcohol **2**, aldehyde **3** and dialdehyde **4**) and demethylation **5** in appreciable yield (Scheme 4). In the presence of higher enzyme activity another metabolite with a high molecular weight was detected, and tentatively assigned as a high molecular weight derivative being a compound possibly emerging *via* a radical coupling pathway. In this case, the presence of radical mediators did not significantly affect the degree of conversion and product distribution. On the other hand, when fully 4-O-methylated model **6** was oxidized under similar experimental conditions only a very low conversion was observed with detection of traces of a dialdehyde derivative **7** (Scheme 4).

The phenolic diphenylmethane and α-5 model structures were found to be remarkably more reactive than the 5-5′ model compounds **1** and **6**, to afford products of side-chain oxidation and demethylation process. Again, the HBT and ABTS mediators did not show any specific reactivity.

In the same study extensive efforts have been made to understand the mechanism of the laccase mediator (LM) system. It has been shown that laccase in the presence of HBT generates the oxybenzotriazolyl radical that can oxidize both phenolic and some non-phenolic lignin models [20] by a hydrogen atom abstraction process rather than an electron transfer process [21]. The oxidation of vanillyl alcohol **8** was then performed with laccase and LM system to further elucidate the role of radical mediators in the modification of phenolic and non-phenolic lignin subunits [22]. The oxidation of **8** with laccase gave **9** and **10**, that are products of alkyl side-chain oxidation and oxidative coupling, respectively (Scheme 5). When HBT was added to the reaction medium, a different behaviour was observed and products of aromatic ring oxidation, *ortho*- and *para*-benzoquinones **11** and **12**, catechol **13** and muconic acid **14** were recovered in appreciable yield.



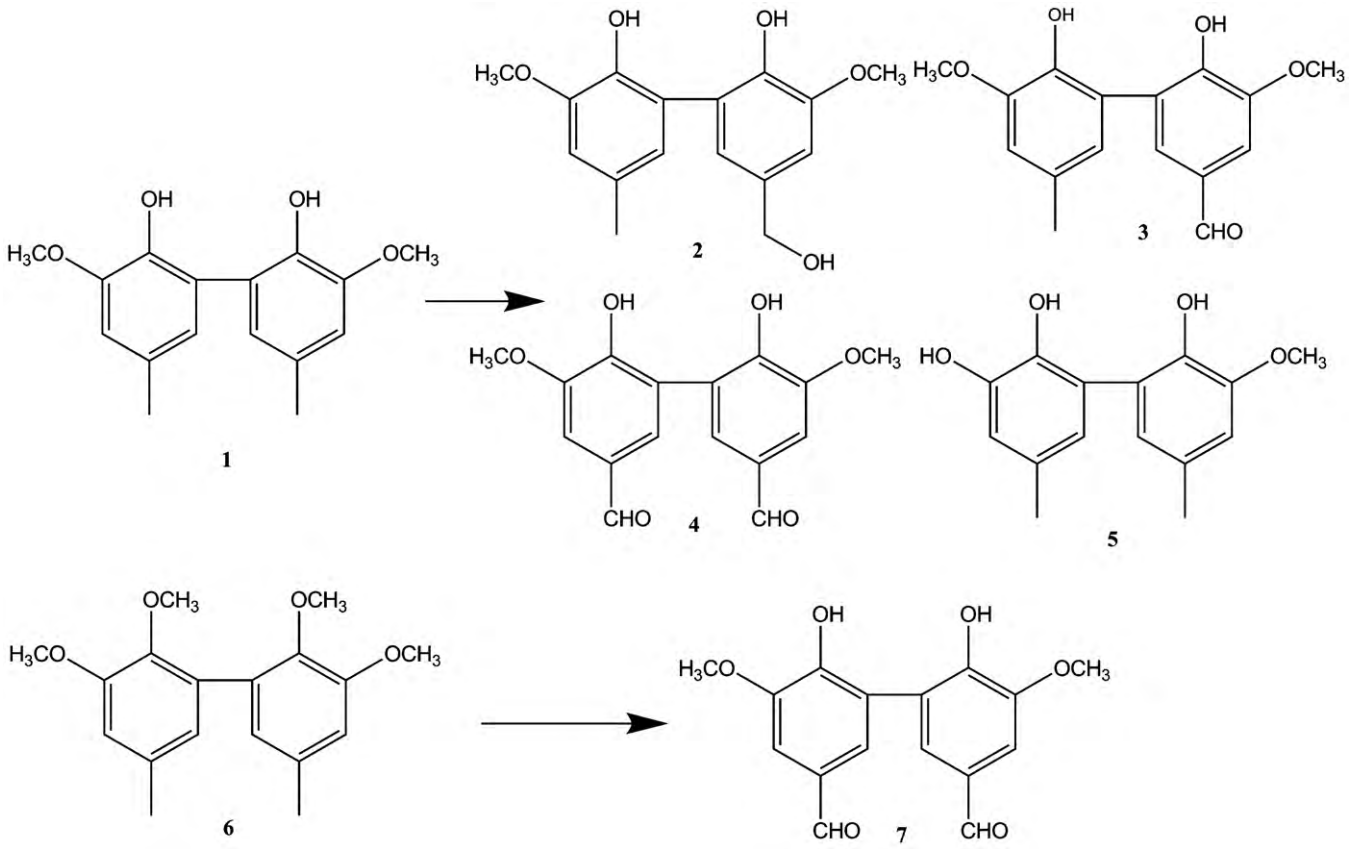
Scheme 3. Laccase oxidation of phenolic compounds. Pathways B, C, D have slow kinetics and are not likely to occur.

The formation of these products cannot be explained on the basis of the reaction of a phenoxy radical with oxygen because the kinetics for oxygen addition to phenoxy radicals are slow [22]. On the contrary, the kinetics of addition of superoxide anion radical to phenoxy radical species are fast and would explain the formation of such a range of products. Calculations were made on the respective bond dissociation energies of the phenolic O–H and benzylic C–H bonds. They showed that in **8** such energies are nearly the same. This could imply that the oxytriazolyl radical could undergo hydrogen atom abstraction at the phenolic and at the benzylic position. This point was better clarified in a recent paper were experimental information acquired after the oxidation of different *para*-substituted phenols with laccase mediators systems, reveals that initial formation of a phenoxyl radical on the one side of the aromatic bifunctional molecule might activate the benzylic substituent on the other side [23]. In this case the benzyl radical produced would undergo fast oxygen addition and superoxide anion radical elimination as reported in Scheme 5. In turn, the superoxide anion radical so generated would react with the phenoxy radical species present in the reaction medium. The laccase mediator system thus not only allows the oxidation of non-phenolic lignin subunits, but allows the formation of superoxide anion radical species that in turn perform the extensive oxidation and aromatic ring cleavage of lignin moieties.

The role of the laccase mediator system was than studied on residual kraft lignin. ^{31}P NMR spectra of lignins, treated with suitable phosphorous derivatising [24–27], after laccase and LM treatments showed the qualitative and quantitative modifications induced on the lignin structures. More specifically it was evident that laccase treatments induced both side-chain oxidation processes (as shown by the decrease of aliphatic O–H groups present in lignin side-chains), and oxidative coupling processes. The last reaction pattern was demonstrated by the increase of condensed phenolic units after the laccase treatment. On the contrary, oxidative coupling reaction pattern, extensive aromatic ring cleavage and alkyl side-chain oxidation were observed when lignin was submitted to LM treatments in the presence of HBT or ABTS.

The industrial use of the laccase or LM system is prevented by both the need to recycle the enzyme and its low stability [28]. There are extensive reports in the literature about laccase immobilization [29–33]. However the main drawback in the application of such protocols lies in the fast deactivation of immobilised laccases. Recently a new process for the deposition of ultrathin multilayer alternatively charged polyelectrolytes onto charged substrates, the layer-by-layer technique (LbL), was developed [34–38].

We used such technique to develop newly immobilised laccases [39]. A first catalyst was prepared by laccase immobilisation onto alumina particles by sylanisation and cross-linking with glutaraldehyde according to classical procedures [30,40]. The immobilised laccase was in turn coated by alternate layers of poly(allylamine) hydrochloride and polystyrene sulfonate (cLbL). The LbL coating of the enzyme resulted in a retained enzymatic activity and in an increased stability with respect to the laccase. In a same fashion LbL poly(allylamine) hydrochloride and polystyrene sulfonate microcapsules were synthesized using a carbonate templates. The core dissolution was followed by the opening of pores onto the micro-

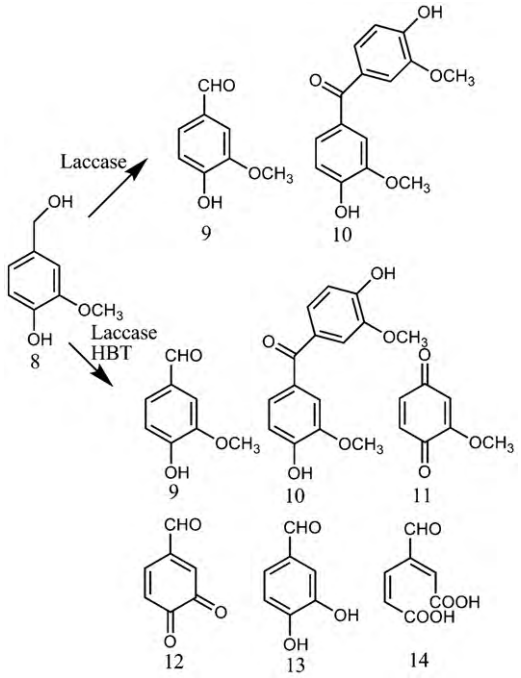


Scheme 4. Enzymatic oxidation of 5-5′ lignin model compounds.

capsules surface by tuning the pH value. At pH 2.8 pores can be opened and the laccase could be loaded inside the microcapsules by coulombic interaction with the oppositely charged polyelectrolyte. Increase in the pH value resulted in the reduction of the pore diameter and enzyme entrapment. The laccase microcapsules (mLbL) showed comparable enzymatic activity and stability than coated laccase particles as shown in Fig. 1.

Both LbL coated laccase particles and microcapsules were studied in the oxidation of lignin with laccase and the LM system [39]. The lignins were oxidized by the immobilised enzymes better than soluble laccase, probably due to the increased stability of the supported enzymes. In the presence of laccase, extensive alkyl side-chain oxidation and aromatic ring oxidative coupling processes were detected as shown by the decrease of the aliphatic OH groups and increase of condensed phenolic units, respectively.

Coated laccase showed a different selectivity than soluble laccase. In fact, while the coated laccase particles undergo extensive side-chain oxidation processes (decrease of aliphatic OH groups in the ^{31}P NMR spectra), the laccase microcapsules catalyze the occurrence of alkyl aryl ether cleavage reactions that yield directly the increase of guaiacyl phenolic units [39].



Scheme 5. Laccase and laccase + HBT oxidation of vanillyl alcohol.

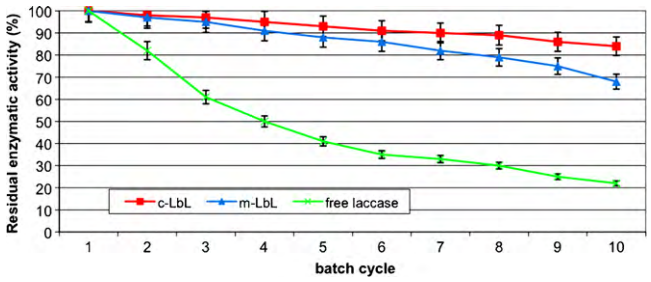
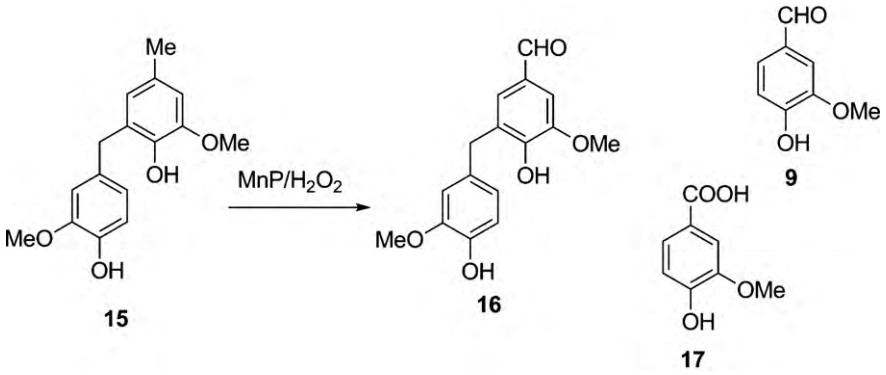


Fig. 1. Laccase, cLbL-laccase and mLbL-laccase residual activity (%) as a function of the number of catalytic cycles. The laccases were allowed to react with ABTS after 10 successive 12 h batch reactions.



Scheme 6. Mn peroxidase oxidation of α-5 lignin model compound **15**.

2.2. Manganese peroxidases

Besides to laccases, Mn-peroxidases (MnP) from white-rot fungi showed a high reactivity in the oxidative functionalisation of lignins [41]. This enzyme, which contains one iron protoporphyrin IX as prosthetic group, is able to activate H_2O_2 in the oxidation of Mn(II) to Mn(III), which in turn, after chelation by organic acids, became a freely diffusible oxidizing species. The ultimate oxidation of lignin is performed by generation of reactive phenoxy radicals through a hydrogen abstraction process [42]. Due to its high reactivity, MnP has been used for the oxidation of different lignin model compounds, including phenolic arylglycerol β-aryl ether [43] and diarylpropane derivatives [44]. Condensed phenolic lignin model compounds, 5-5′, β-5 and diphenylmethane subunits were also efficiently oxidized by MnP [45]. In particular, when the 5-5′ model compound **1** was treated with MnP produced by the white-rot fungus *Lentinula edodes* [46], an extensive conversion of substrate was obtained to yield products of alkyl side-chain oxidation, including the corresponding benzyl alcohol **2** and aldehyde **3**. In addition, trace amounts of a demethylation product **5** were found (Scheme 4).

It is interesting to note, that the β-5 lignin model compound, 2,4′-dihydroxy-3,3′-dimethoxy-5-methyl-diphenylmethane **15**, was the most reactive substrate during MnP/H_2O_2 oxidation to afford products of alkyl side-chain oxidation **16** and oxidative cleavage of the carbon bridging position, that are vanillin **9** and vanillic acid **17** (Scheme 6).

These results clearly suggest that the oxidation is selective for the methyl or methylene groups in *para*-position to OH moieties. In the case of the methylene moiety, the cleavage of the carbon bridging position became an operative process.

3. Modification of fibers by laccases and plasma procedures

3.1. Radicalization of fibers by laccase treatments

Several studies on the action of oxidative enzymes on fiber bound lignin and on low molecular weight lignin model compounds have been reported [47–50]. The effects of laccase on fiber bound lignin have been most commonly monitored by measuring the consumption of the co-substrate *i.e.* oxygen, by monitoring the effects of the oxidation on the physical properties of fibers or by studying the formation of radicals [51,52]. In order to study the formation of radicals and the concentration of radicals on lignin, a milled wood lignin (MWL) suspension was treated with laccase, for 2 h. Aliquots of the reaction solutions were taken at increasing reaction times and the amount of radicals in the samples were detected. No detectable EPR signals were found in the reference treated samples. As expected, after laccase treatment of MWL samples EPR

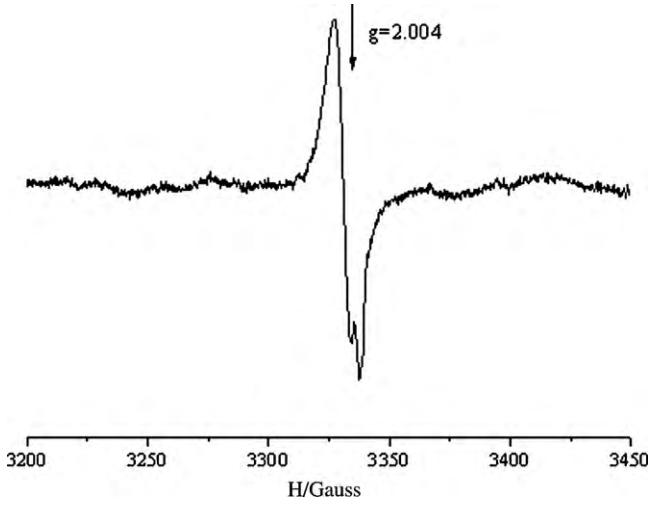


Fig. 2. X-band EPR spectrum recorded at 123 K on TMP fibers after oxidation in water in the presence of laccase at 1 bar O_2 pressure for 60 min.

signals typical of phenoxy radicals ($g = 2.004$ and $\Delta Hpp = 9$ G) were observed as reported by Hon (Fig. 2) [53].

The concentration of radicals during the laccase treatment was found to be rather constant (Fig. 3) [54].

Laccase reacts primarily with the phenolic hydroxyl groups and form the corresponding radicals. Laccases can be also used to activate the surface lignin of lignin-rich pulps. Some example of fiber activation is reported in the literature. For example thermomechanical pulps, TMPs [55], medium density fiber-board fibers, MDF [56], and kraft pulps with various kappa numbers [57] have been the target for laccase oxidation. From the mechanistic point of view a linear correlation between the radical formation and oxygen consumption in beech wood fibers has indeed been reported [56]. In mechanical pulp, this correlation has not, how-

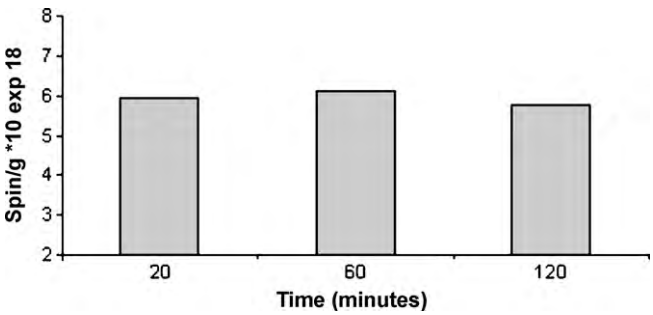


Fig. 3. Phenoxy radicals generated by laccase treatments in MWL.

ever, always been confirmed [55]. Recently it was demonstrated that the laccase was found to have higher reactivity with the pulps containing more accessible and reactive surface lignin. The reactivity of the pulps towards laccase oxidation, as evaluated by EPR spectroscopy, increased in the order TMP < CTMP < SWKP ~ HWKP. The time needed for the maximum radicalization of pulp fibers was dependent on the pulp type [58]. Other factors affecting the concentration of radicals on lignin in lignocellulosic fibers are the laccase dosage the pH and also the amount and type of LMWC present in pulp affect the activation efficiency of wood pulps fibers. All theses factors need to be taken into consideration and optimised when aiming at the optimal activation of a pulp material.

3.2. Fibers radicalization by plasma treatments

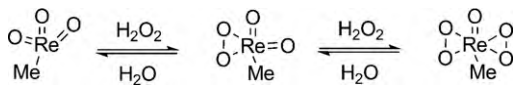
A promising alternative technique for obtaining high amounts of radicals in fibers employs plasma, which allows avoiding long reaction times and the use of solvents. The plasma state can be divided into two main categories: hot plasmas and cold plasmas. For our purposes only cold plasma could be useful. Cold plasmas (non-equilibrium plasmas) are composed of energetic electrons and low energy neutral and charged species. Due to the low caloric capacity of the electrons, cold plasma treatments have proven to be suitable for modifications of organic materials because the substrate remains at, or near room temperature. Moreover, cold plasma techniques are dry, clean processes without environmental concerns. For these reasons, in the last years plasma treatments were performed on different materials for many purposes [59,60], about lignin radicals formed at the surface of jute lignocellulosic fibers after cold Ar plasma treatments were studied [61,62] and it was demonstrated that lignin is the primary molecular site of radical formation. In a study published in 2005 [63] was demonstrated that Ar plasma treatment of fibers obtained from chemical pulp (softwood kraft fibers) and of CTMP fibers forms a higher concentration of phenoxy radicals than enzymes, leading to a modification of the lignin chemical structure, as assessed by Nuclear Magnetic Resonance spectroscopy (^{13}C NMR) and Gel Permeation Chromatography (GPC). These results were successively confirmed and assessed [64]. It was demonstrated that the maximum concentration of phenoxy radicals in CTMP fibers triple their concentration after cold Ar plasma treatment in only 60 s at 0.4 mbar, a much shorter time than that required in the case of wet methods. After 60 s of treatment, the concentration of radicals does not change any more, suggesting that the formation of phenoxy radicals competes with their coupling.

4. Organometallic catalysis for the oxidation of lignins and lignin model compounds

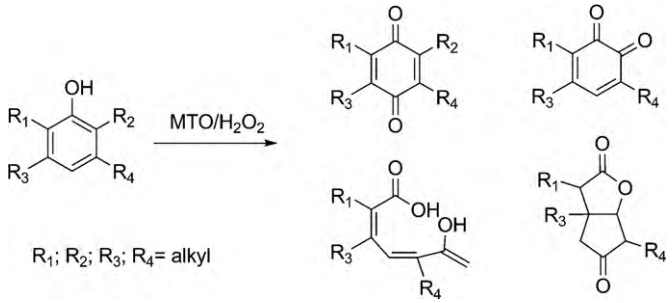
4.1. Catalysis by MTO

Methyltrioxo rhenium (MTO) is the simplest organometallic compound containing Re(VII). In recent years, MTO has been used in several organic transformations including the selective oxidation of natural substances with hydrogen peroxide (H_2O_2) as environmental friendly oxidant [65,66]. The activation of H_2O_2 by MTO requires the formation of two peroxorhenium intermediate, a monoperoxo [$MeRe(O_2)O_2$] and a bis-peroxo [$MeRe(O_2)_2O$] η^2–rhenium complexes (Scheme 7) [67], which reactivity and stability strictly depends on the specific conditions applied for the transformation.

The transfer of the oxygen atom from these peroxo-η^2–rhenium complexes to a substrate is achieved by a butterfly-like transition state through a concerted mechanism without formation of intermediate radical species. The oxidation of polyphenol derivatives



Scheme 7. Reaction of $MeReO_3$ with hydrogen peroxide.



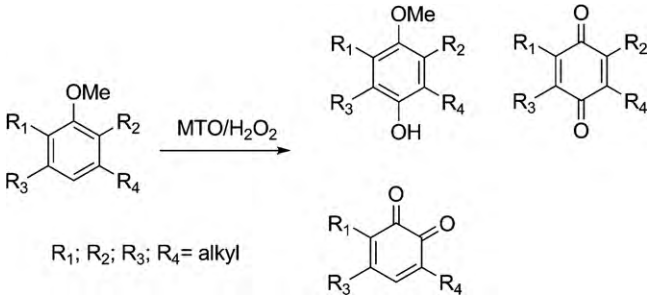
Scheme 8. Oxidation of substituted methoxy benzenes by $MeReO_3/H_2O_2$. Aromatic ring cleavage products.

usually requires drastic experimental conditions with high excess of toxic stoichiometric oxidants [68]. MTO is able in mild conditions to activate H_2O_2 for the oxidation of substituted phenols and methoxybenzene derivatives to corresponding benzoquinones, some of which are characterized by important biological activities [69,70]. The reaction usually involves the formation of arene oxide intermediates and successive nucleophilic ring opening with rearrangement processes [71]. The oxidation of alkyl substituted phenols with the MTO/H_2O_2 system affords both *ortho*- and *para*-benzoquinone isomers depending on the steric hindrance and position of the substituents on the aromatic ring, the presence of bulky alkyl substituents in the C-2 position favouring the formation of 1,4-benzoquinones [72]. In some cases, products of over-oxidation and successive ring opening of the benzoquinone moiety, such as muconic acid derivatives and di-γ-lactones, were also observed (Scheme 8) (for an example of oxidative cleavage of natural phenols with MTO see reference [73]).

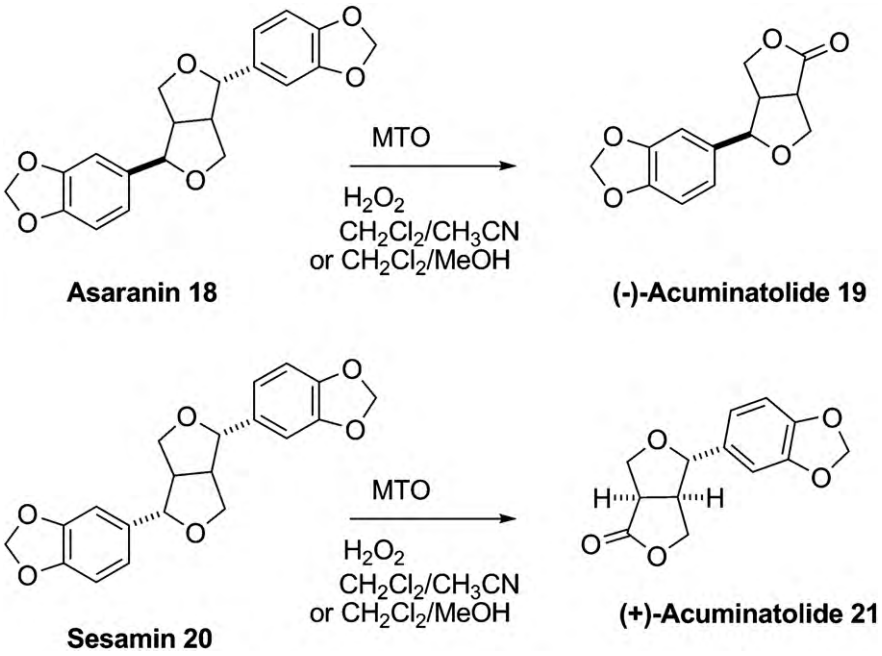
The oxidation of methoxybenzene derivatives with MTO/H_2O_2 system also affords benzoquinones besides to products of hydroxylation of the aromatic ring and of oxidative demethylation (Scheme 9) [69,74].

Recently, studies on the oxidation of both lignan and neolignan derivatives with MTO and H_2O_2 have been performed to evaluate the potentiality of this catalyst system in the oxidative functionalisation of lignins (for a definition of lignin and neolignans see reference [75]).

As an example, tetrahydrofurofuran lignans, asaranin **18** and sesamin **20**, are selectively dearylated to acuminatolide stereoisomers **19** and **21** respectively by simple treatment with MTO and H_2O_2 in CH_2Cl_2/CH_3CN or CH_2Cl_2/EtOH mixtures at room temperature (Scheme 10) [76].



Scheme 9. Oxidation of substituted methoxy benzenes by $MeReO_3/H_2O_2$.



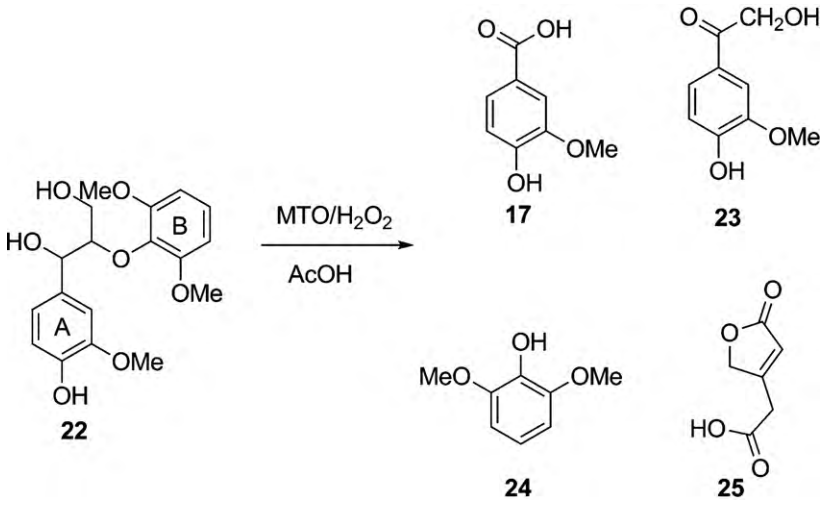
Scheme 10. Selected example of oxidative dearylation of tetrahydrofurofuran lignans; the case of asaranin.

The reaction proceeded through the initial oxidation of the benzylic position by diastereoselective oxygen atom insertion into the C–H bond, followed by ring opening of the hydroxyl-furane moiety, Baeyer–Villiger rearrangement and formation of the lactone moiety.

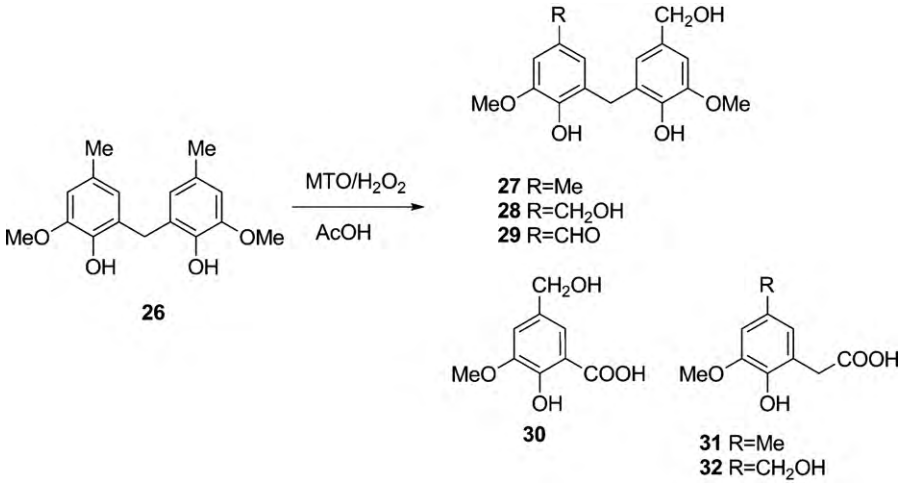
The high diastereoselectivity observed was explained on the basis of the different stability of two competitive transition states during the first oxygen atom transfer process, due to a preferential π-interaction between MTO and the aromatic moiety on the exo face of the tetrahydrofuran ring. Furan and butyrolactone lignans, representative of chemical networks in lignins, are also efficiently oxidized by MTO/H_2O_2 system [77,78].

To further modeling the complexity of the structure of lignin, a selected array of monomeric phenols and dimeric neolignans resembling the main bonding patterns in native and technical lignins was studied [79]. Phenolic and non-phenolic monomeric model compounds, vanillyl alcohol and veratryl alcohol (not shown), treated with MTO/H_2O_2 system in acetic acid (ACOH) yielded a complex mixture of products including derivatives of side-chain oxidation (both aldehydes and carboxylic acids) and of the aromatic moiety. In this latter case, benzoquinones and muconolactones, derived from oxidative ring cleavage of the aryl group were detected in significative yield. Similar results were observed in the case of more complex β-O-4 dimeric compounds, such as 1-(4-hydroxy-3-methoxyphenyl)-2-(2,6-dimethoxyphenoxy)propane-1,3-diol **22**. In this case products of alkyl side-chain oxidation and successive cleavage at the α-position or at the β-position, namely compounds **17**, **23** and **24**, and product of aromatic ring oxidation **25**, were recovered (Scheme 11).

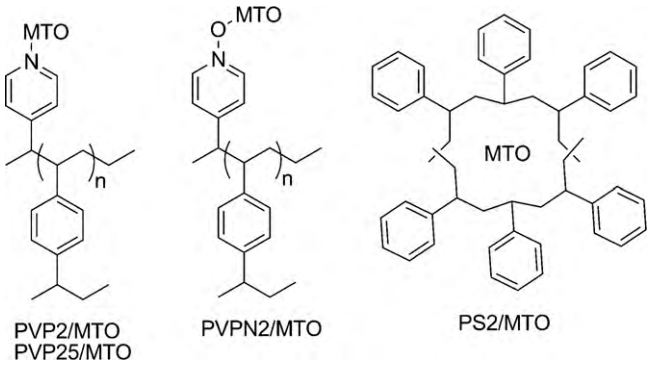
Diphenylmethane neolignans [80] were oxidized by MTO/H_2O_2 system in ACOH. More specifically compound **26** afforded products of side-chain oxidation **27**–**29**, cleavage of the diphenylmethane bridge **30** and of extended oxidative cleavage of one of the aromatic ring as shown by the presence of products with two carbon-atoms in the side-chains **31** and **32** (Scheme 12).



Scheme 11. $MeReO_3/H_2O_2$ oxidation of a β-O-4 aryl ether lignin model compound **22**.



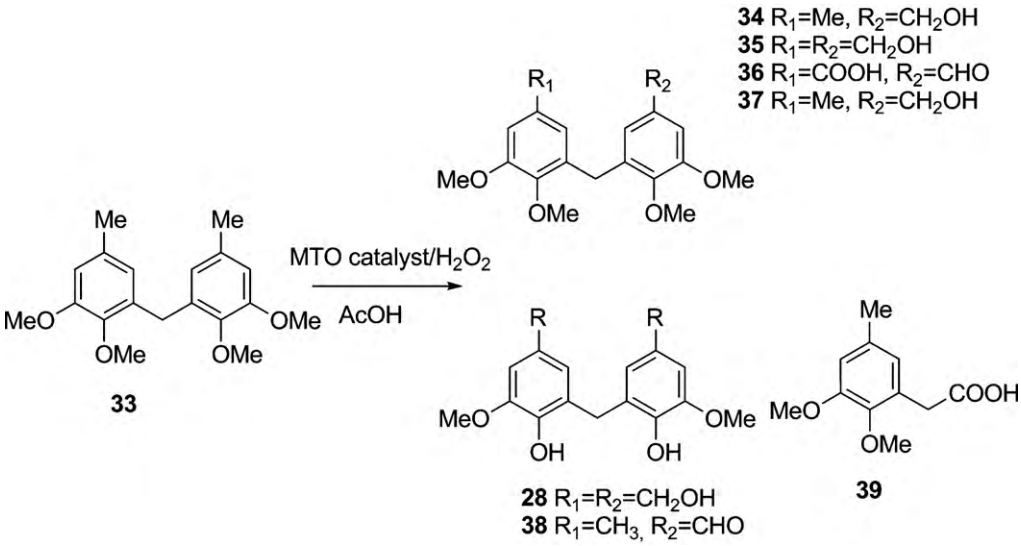
Scheme 12. $MeReO_3/H_2O_2$ oxidation of a phenolic diphenyl methane lignin model compound **26**.



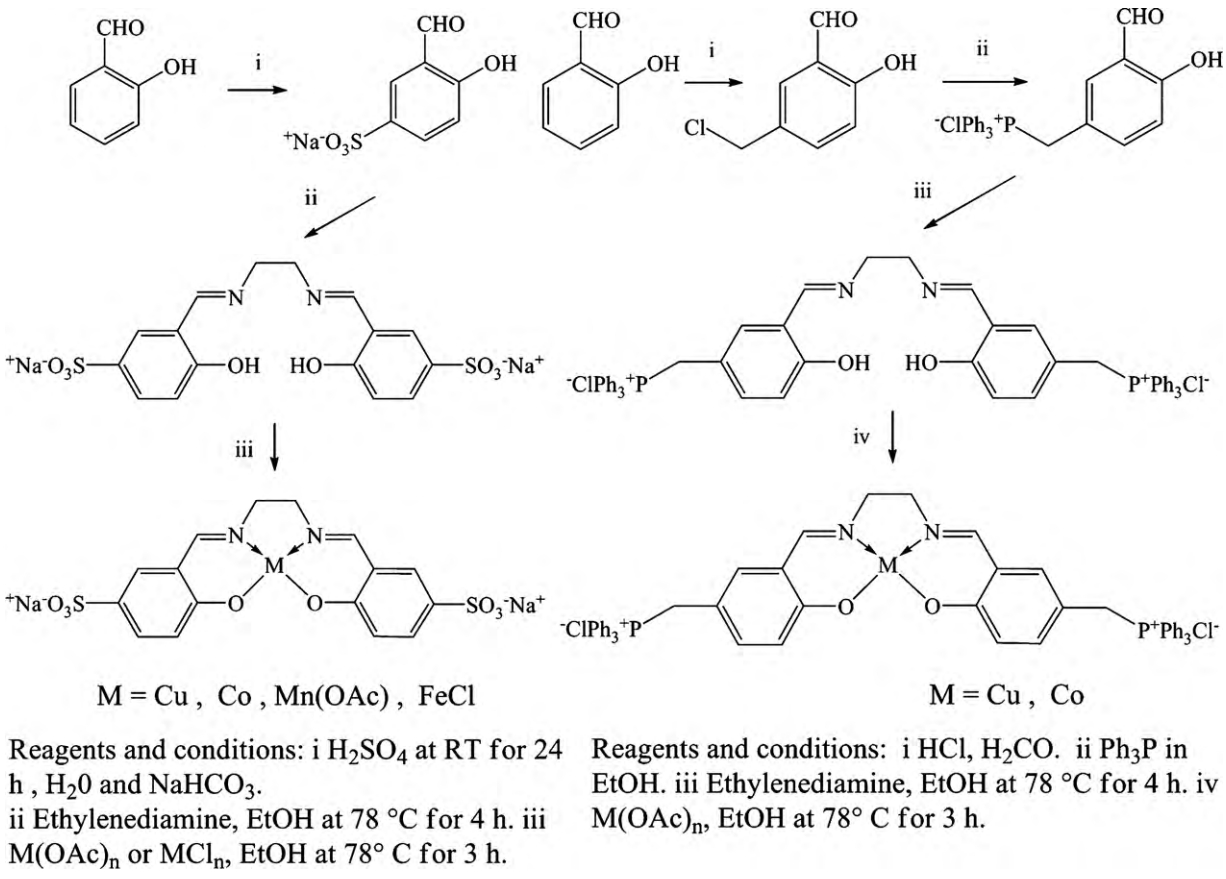
Scheme 13. Structures of MTO poly(4-vinylpyridine) 2% and 25% cross-linked/MTO (PVP/MTO) and PVP25/MTO, and poly(4-vinylpyridine-*N*-oxide) 2% cross-linked/MTO (PVPN2/MTO) and microencapsulated polystyrene 2% cross-linked/MTO (PS2/MTO).

The procedures for the oxidative functionalisation of lignin model compounds have been also applied to lignins. Hydrolytic sugar cane lignin (SLC), red spruce kraft lignin (RSL) and hardwood organosolvent lignin (OSL), that are all representative of widely diffused *para*-hydroxyphenyl-guaiacyl, guaiacyl-syringyl and simple guaiacyl lignins, have been oxidized with MTO/H_2O_2 system in ACOH at room temperature. The selectivity of the oxidation was studied by means of advanced ^{31}P NMR techniques that allow the quantitative determination of all OH moieties after phosphitylation of the sample with 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane in the presence of a known amount of cholesterol as an internal standard [25,26]. Irrespective to the specific lignin studied, an extensive modification of the polymer was observed, including alkyl side-chain oxidations (with a relevant decreases of aliphatic OH groups), aromatic ring cleavage (suggested by the increases of COOH content) and decrease of recalcitrant condensed units (more than 67% and 60% with SLC and RSL, respectively). The modifications occurred on the lignin samples are in accord with the above reported reactivity of model compounds. Moreover, the formation of highly functionalised lignin fragments was reported.

The oxidation of lignin and lignin model compounds was successively performed with heterogeneous rhenium catalysts based on the heterogenation of MTO on low cost, no toxic and easily available polymeric support, such as poly(4-vinylpyridine) (PVP) or polystyrene (PS) [81], applying the "mediator concept" and the microencapsulation technique [82]. The structures of



Scheme 14. $MeReO_3/H_2O_2$. oxidation of a non-phenolic diphenyl methane lignin model compound **33**.



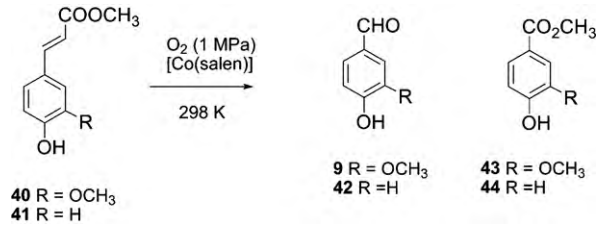
Scheme 15. Salen synthesis.

MTO heterogeneous catalysts employed for the oxidation, namely poly(4-vinylpyridine) 2% and 25% cross-linked/MTO (PVP/MTO) and PVP25/MTO, respectively, and poly(4-vinylpyridine-*N*-oxide) 2% cross-linked/MTO (PVPN2/MTO), besides to microencapsulated polystyrene 2% cross-linked/MTO (PS2/MTO), are schematically represented in Scheme 13.

The oxidation of monomeric and dimeric lignin model compounds, carried out by treating the appropriate substrate with H_2O_2 and supported catalysts (containing 1.0% w/w of the active MTO) in ACOH proceeded with a selectivity similar to that observed for MTO alone, yielding products of alkyl side-chain oxidation, oxidative ring opening of the aromatic moieties and oxidation to benzoquinone derivatives [83]. On the other hand, the mass balance measured for heterogeneous oxidations was significantly higher than that obtained with MTO, suggesting that the supports are able to tune the reactivity of rhenium avoiding the formation of over-oxidation products (for a general study on the effect of the resin on the selectivity of MTO see reference [84]). The oxidation was operative also in the case of diphenylmethane dimeric lignin model compounds. As for example, the oxidation of non-phenolic diphenylmethane lignin model compound **33** afforded products of alkyl side-chain oxidation to benzyl alcohol **28**, **34** and **35**, aldehyde **36** and **37**, demethylation at the alkyl-arylether moieties **28** and **38**, and oxidative ring cleavage of one of the aromatic rings **39** (Scheme 14).

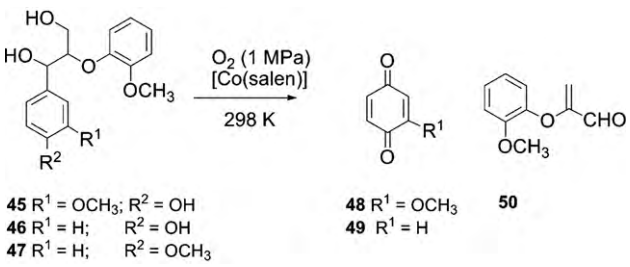
4.2. Catalysis by Co salen complexes

Salen complexes are an important class of organometallic compounds, which have been used since 1933 to catalyze a wide variety of reactions [85]. Many of these reactions are oxidations of organic substrates with oxidants like O_2 and H_2O_2. The synthesis of water or organic solvent-soluble salen complexes is simple, easy and economic as reported in literature from Sipila et al. [86] (Scheme 15).

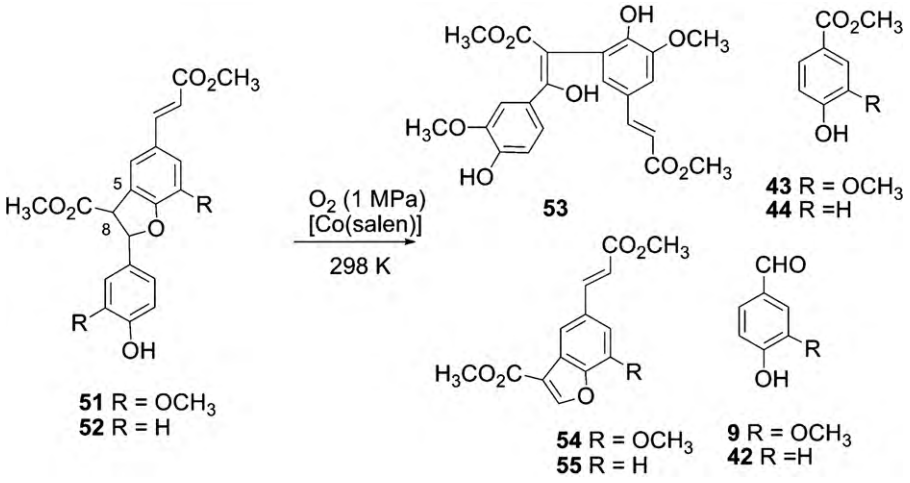


Scheme 16. Co(salen)/O_2 oxidation of cynnamic esters.

For these reasons, they can be used as catalysts in the field of lignin and wood chemistry. In particular it was demonstrated that they were able to oxidize in high yields lignin model compounds.



Scheme 17. Co(salen)/O_2 oxidation of phenolic and non-phenolic β-O-4 aryl ether lignin model compounds **45**, **46** and **47**.



Scheme 18. Co(salen)/O_2 oxidation of phenolic and non-phenolic β-5 lignin model compounds **51** and **52**.

Arylglycerol-β-aryl ethers **45**, **46** and **47**, phenylcoumarans **51** and **52** and apocynol showed very high conversion values within 30 min from reaction onset and their conversion rates were higher than those reported for phenylpropenoidic compounds, such as *E*-methyl ferulate **40** and methyl *E*-4-hydroxycinnamate **41**. The distribution of the main aromatic products **42**–**44** and **48**–**50**, 48 h from the onset of oxidation in chloroform of the lignin phenyl propenidic and arylglycerol-β-aryl ether lignin model compounds is reported in Schemes 16 and 17 respectively.

Schemes 18 shows the oxidation products **43** and **44**, **53**–**55**, **9** and **42** obtained from Co salen treatments of phenylcoumaran model compounds.

For the oxidation of monomeric and dimeric lignin model compounds with oxygen catalyzed by [Co(salen)] [87–89], the reactivity and the characterization of radical intermediates by electron paramagnetic resonance (EPR) spectroscopy suggested that such oxidation occurs through the following three steps:

$$[Co^{II}(salen)] + ROH + E_2 \rightleftarrows [Co^{III}(salen)(ROH)(O_2^-)] \quad (1)$$

$$[Co^{III}(salen)(ROH)(O_2^-)] + ROH \rightleftarrows [Co^{III}(salen)(ROH)(RO^\bullet)] + HO_2^- \quad (2)$$

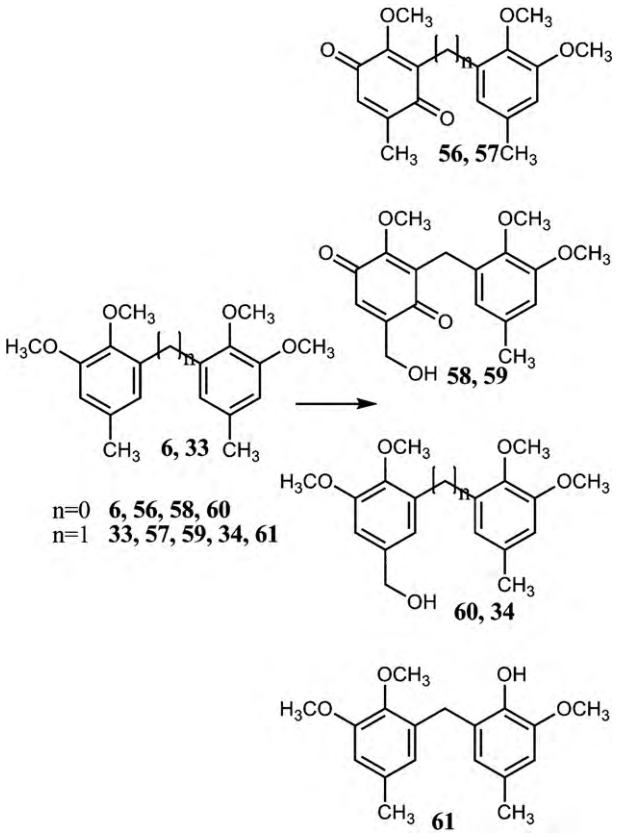
$$[Co^{III}(salen)(ROH)(RO^\bullet)] + HO_2^- \rightleftarrows [Co^{III}(salen)(RO^-)(RO^\bullet)] + H_2O_2 \quad (3)$$

where ROH is the phenol unit and RO• the corresponding radical.

For the single reaction steps:

(1) the superoxocobalt derivative, $[Co^{III}(salen)(ROH)(O_2^-)]$, formed by electron transfer from $[Co^{II}(salen)]$ to O_2;
(2) further reduction of O_2^- to HO_2^- occurs, together with the cobalt coordination of a second ROH molecule as RO•, giving the phenoxy cobalt radical $[Co^{III}(salen)(ROH)(RO^\bullet)]$;
(3) one ROH ligand loses H^+, leading to the formation of the phenoxy-phenate cobalt radical $[Co^{III}(salen)(RO^-)(RO^\bullet)]$.

After the third step, RO• probably dissociates from the cobalt center, and then further reacts with O_2 giving oxidized molecular products. It was expected that lignocellulosic fibers might undergo radical formation under similar oxidative conditions so that they can be activated towards interesting morphological and structural modifications. In this context, the radicals formed on unbleached fibers obtained from thermomechanical (TMP) and chemothermomechanical (CTMP) pulps after reaction with oxygen, using [Co(salen)] as catalyst have been identified and quantified by EPR spectroscopy. Both materials are rich in lignin and are widely used for industrial purposes. Unbleached CTMP has a slightly higher surface content of lignin than unbleached TMP [90,91], and some sulphonate groups are grafted to the lignin during manufacture of CTMP [92,93]. After treatment with molecular oxygen in methanol in the presence of [Co(salen)], TMP fibers formed a higher amount of radicals and in parallel underwent deeper structural and morphological changes than CTMP [94]. In the same experimental conditions, by using [Co(salen)] as catalyst, the absolute amount



Scheme 19. Manganese and iron *meso*-tetra(2,6-dichloro-3-sulphonatophenyl) porphyrin chloride (TDCSPPMnCl and TDCSPPFeCl, respectively) and *meso*-tetra-4-sulphonatophenyl porphyrin chloride (TSPPMnCl), and manganese *meso*-tetra(*N*-methylpyridinio)porphyrin pentacetate TPyMePMn(MeCOO)$_5$ oxidation of non-phenolic diphenylmethane and diphenyl lignin model compounds **6** and **45**.

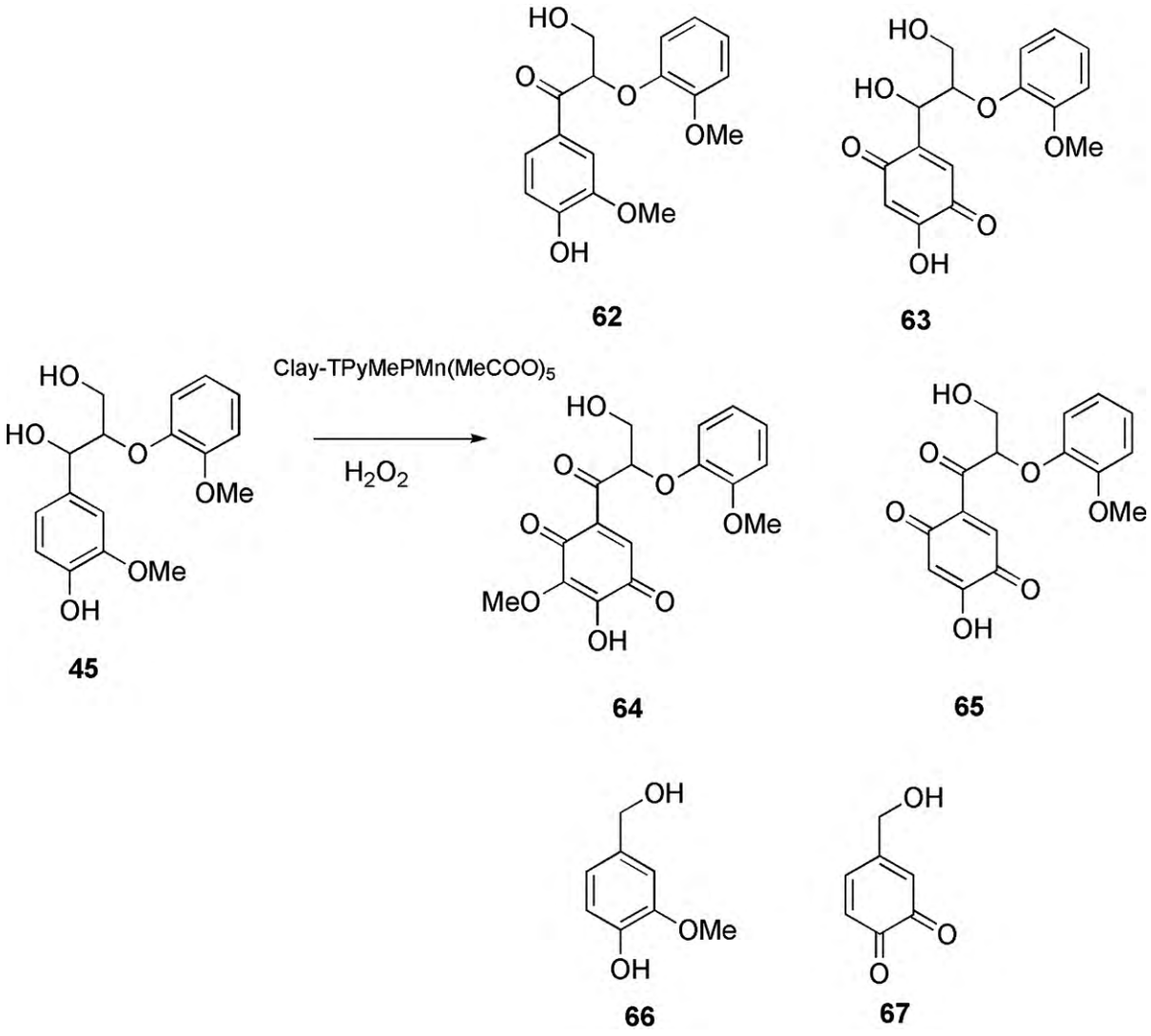
of radicals in fibers reaches very high values, 10 times higher than those reported in the literature for the treatment with laccase and molecular oxygen of TMP and of milled wood lignin (MWL) [94]. These results are probably due to the smaller molecular dimension of [Co(salen)] compared with laccase, which allows the catalyst to interact also with subsurface lignin phenol groups. The results of EPR investigation showed that the oxidation of unbleached TMP fibers by molecular oxygen, catalyzed by [Co(sulphosalen)] [95] in water, induced the formation of phenoxy radicals that were very similar to those reported in the literature for the treatment of the same fibers with molecular oxygen and laccase [58]. By contrast, in the presence of [Co(salen)] in methanol, phenoxy cobalt radicals similar in structure to those formed during the oxidation of lignin model compounds were observed After 60 min of reaction, the amount of radicals formed on TMP fibers in the presence of either [Co(salen)] or [Co(sulphosalen)] did not significantly differ. This result suggests that that efficient radical formation on fibers can be achieved also in water with water-soluble catalysts.

The obtained results showed that the treatment with molecular oxygen in the presence of [Co(sulphosalen)] in water represents a promising way to approach an environmentally sustainable radical formation on fibers, without an heavy modification of the lignin structure.

5. Oxidative functionalisation of lignin and lignin model compounds by biomimetic catalysis

5.1. Catalysis by metalloporphyrins

The selective modification of lignin in wood is mainly accomplished by enzymes produced by white-rot basidiomycetes, such as laccases, lignin peroxidases (LiP) and manganese dependent peroxidases (MnP) [96]. The enzymes LiP and MnP are able to activate H_2O_2 as primary oxidant involving the protoporphyrin IX (iron-PPIX) as the active site. The catalytic cycle is characterized by a two electron oxidation process of Fe(III) protoporphyrin IX to give a reactive oxo-iron (IV) protoporphyrin IX π-cation radical, namely the LiP I complex. This reactive intermediate is then reduced to the initial state by two one-electron reductions of the substrate involving the formation of intermediate LiP II. Unfortunately, when exposed to an excess of H_2O_2, LiP is inactivated by over-oxidation to LiP III, thus limiting the industrial applications [97]. Synthetic metalloporphyrins are biomimetic catalysts for LiP and MnP, because they can yield highly oxidized metallo-oxo species similar to LiP I and LiP II [98]. Highly functionalised porphyrins bearing aryl substituents in the *meso* positions of the ring are catalyst systems stable to oxidants, and their redox potential, as well as their solubility, can be finely tuned by the stereo-



Scheme 20. TPyMePMn(MeCOO)$_5$/clay/H_2O_2 oxidation of a β-O-4 aryl ether lignin model compound **45**.

electronic properties of the substituents. For example, recalcitrant residual kraft lignin and 5-5′ diphenylmethane substituents have been oxidized with H_2O_2 and an array of anionic manganese and iron *meso*-tetra(2,6-dichloro-3-sulphonatophenyl) porphyrin chloride (TDCSPPMnCl and TDCSPPFeCl, respectively) and *meso*-tetra-4-sulphonatophenyl porphyrin chloride (TSPPMnCl), and cationic manganese *meso*-tetra(*N*-methylpyridinio)porphyrin pentacetate TPyMePMn(MeCOO)$_5$, working in buffer in the range of values of pH 3–6. Irrespective to experimental conditions, the oxidation of the dimeric model compounds **6** and **33** afforded products of aromatic ring oxidation to benzoquinones **56** and **57**, alkyl side oxidation **58**, **59**, **34**, **60** (benzyl alcohol derivatives), and demethylation **61** (Scheme 19).

A comparison between TDCSPPMnCl and TDCSPPFeCl, showed that the manganese porphyrin was able to perform a more extensive oxidation than the iron one. The anionic porphyrin TSPPMnCl was the less active catalyst while TPyMePMn(Me$_3$COO)$_5$ showed a higher conversion rate at pH 3 than pH 6. The distribution of aliphatic, phenolic and carboxylic hydroxyl groups in residual kraft lignin before and after porphyrins catalyzed oxidation was evaluated by ^{31}P NMR spectroscopy. As a general reaction pattern a decrease of aliphatic OH groups was detected, according to the occurrence of side-chain oxidations along with the increase of COOH units and a significative variation in the amount of phenolic groups [99]. A different selectivity was also observed depending on the nature of the catalyst. Thus, manganese porphyrins were more efficient in carrying-out the oxidative process producing only a low amount of coupling reactions, as suggested by the presence of low amount of condensed phenolic OH groups. The comparison between anionic and cationic water soluble Mn porphyrins TSPPMnCl and TPyMePMn(MeCOO)$_5$, respectively, showed an increased efficiency in the case of the cationic catalysts. A further step in the design of robust biomimetic catalysts of LiP based on metalloporphyrins was the immobilization procedure of active species on inorganic supports that mimic the effect of the polypeptide envelope to protect the catalytic center toward deactivation. In principle these catalytic systems can be recovered by filtration from the reaction mixture and used for successive runs. Among the different support tested, clays of the smectite family, such as montmorillonites, have been used to immobilize cationic metalloporphyrins used in the oxidation of lignin and lignin model compounds [99]. In fact, montmorillonites have a complex layer lattice structure in which two-dimensional oxyanions are separated by layers of hydrate metal cations that can be substituted by organic cationic active species utilizing simple ion exchange methods [100,101].

In this context, the cationic porphyrin TPyMePMn(MeCOO)$_5$ was efficiently immobilized on montmorillonite to yield a novel heterogeneous TPyMePMn(MeCOO)$_5$/clay catalyst and applied for the oxidation with H_2O_2 of a series of lignin model compounds.

As for example, the β-O-4 arylglycerol phenyl ether model compound **45** was treated with the TPyMePMn(MeCOO)$_5$/clay/H_2O_2 catalyst system in dioxane/citrate buffer at 60 °C to yield products of side-chain oxidation **62**, para-benzoquinone formation **63**, side-chain oxidation and quinone formation **64** and **65**, and prod-

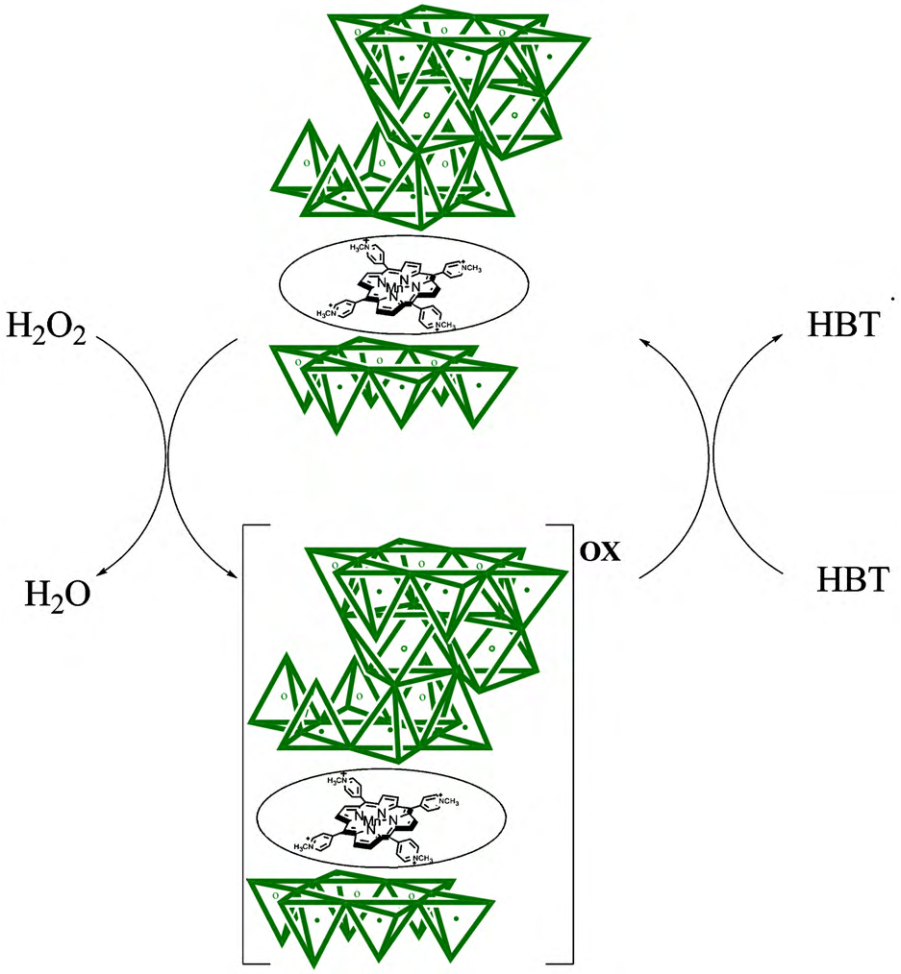


Fig. 4. Reactivity pathway of the TPyMePMn(MeCOO)$_5$/clay mediator system.

ucts of side-chain cleavage **66** and side-chain cleavage and quinone formation **67** (Scheme 20).

Since the mass balance was not quantitative, the formation of water soluble low molecular weight fragments was also an operative process. A similar reactivity was obtained also in the case of diphenyl methane lignin model compounds. This behaviour implies a potential delignification effect in view of the depolymerization process of lignin. On the other hand, in view of the application of heterogeneous biomimetic catalysts, like TPyMePMn(MeCOO)$_5$/clay, to lignins, some problems due to presence of kinetic barriers for the approach of the polymer to active metal site require to be evaluated. With the aim of solving this problem, the TPyMePMn(MeCOO)$_5$/clay catalyst was used in the presence of veratryl alcohol (VA) and 1-hydroxybenzotriazole (HBT) as diffusible low molecular weight redox mediators, thus designing a completely new clay–porphyrin mediator system (clay–PMS). In this biomimetic system, the redox mediator acts as a shuttle of the oxidation, being first oxidized by the active metal center and then diffusing the redox potential outside the clay matrix to lignin (Fig. 4) [95]. In particular, the clay–PMS catalyst system was applied to oxidative functionalisation of Black Spruce milled wood (MWL) and residual Kraft (RKL) lignins, with H_2O_2 in buffer citrate phosphate (pH 6) and, when necessary, in the presence of the appropriate redox mediators.

As revealed by ^{31}P NMR spectroscopy, the treatment of MWL with both clay–PMS/redox mediators yielded a relevant decrease in aliphatic OH groups, while reference systems TPyMePMn(MeCOO)$_5$/clay and simple clay–PMS were not efficient catalysts, thus confirming the role of HBT and VA in the oxidation. Moreover, the reaction performed with HBT was more efficient than that with VA, probably because of a higher stability of HBT radical. It is worth to note, that possible oxidative coupling reactions were not observed during the treatment of lignins. In agreement with an extensive oxidation of the MWL polymer, the number of guaiacyl OH groups decreased, and that of COOH moieties increased, in the presence of both redox mediators. Similar results were observed during the oxidation of RKL suggesting that the clay–PMS/redox mediator represent one of the last step in the development of metalloporphyrins based "synthetic LiP" useful for extensive lignin modification and functionalisation.

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